Course Faculty:

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Course credits: 3  
Class hours: Spring 2015; Wednesdays 2pm-5 pm, Rm HPNP 2306  
Pre-/Co-requisites: Biostatistics, Epidemiology Methods, or permission of the instructor.  
The enrollment in the course is limited, so graduate students have priority over advanced professional students.

Course Description:

Pharmacoepidemiology and the Science of Drug Safety play an important role in drug safety, drug effectiveness, outcome assessment, and regulatory decision-making. Although randomized clinical trials are considered the recommended approach in testing drug efficacy, often, drug safety issues are addressed with observational study designs, including patient follow-up studies, case-control and cohort designs.  
Advances in clinical databases facilitate the conduct of large-scale cohort studies and nested case-control studies. Since the economic impact of pharmacoepidemiology studies is significant, sound methodological approaches are needed.  
The US FDA introduced the concept of Therapeutic Risk Management, which allows restricted marketing of designated drugs so that a positive benefit/risk balance is maintained.

Course Objectives and Readings:

Behavioral Outcome Objectives:

- Recognize drug safety issues and develop appropriate strategies to optimize the benefit/risk ratio of the product involved  
- Be able to write a study protocol in a clear, simple, and parsimonious manner, responsive to the question at hand, and propose a methodological sound design

Course Texts and Readings:

Recommended Texts:
Hartzema AG, Tilson HH and Chen A. *Pharmacoepidemiology and Therapeutic Risk Management*. Harvey Whitney Press, Inc. Cincinnati 2008. (Your instructor for this course does not receive any royalty from the book.)

**Useful Websites:**
International Society of Pharmacoepidemiology and Therapeutic Risk Management (ISPE)-
http://www.pharmacoepi.org/
Food and drug Administration(FDA)  www.fda.gov
Pharmaceutical Research and Manufacturers Administration (PhRMA) http://www.phrma.org/
iMeds http://imeds.reaganudall.org/  (OMOP historical files)
Mini-Sentinel http://www.mini-sentinel.org/
National Institute for Clinical Excellence (NICE)  www.nice.org.uk
COCHRANE GROUP  www.cochrane.org
Site matches patient’s profiles to enrollment criteria for cancer trials http://www.emergingmed.com/
National Institute of Health (NIH) registration of clinical trials http://www.clinicaltrials.gov/
CenterWatch Additional source of clinical trial information http://centerwatch.com/
Website Searches multiple websites for listing, trial results and trial news http://searchclinicaltrials.org/
http://www.gsk-clinicalstudyregister.com/
Clinical Trial data as posted by the industry.  https://clinicalstudydatarequest.com/
OHDSI Observational Health Data Sciences and Informatics  http://www.ohdsi.org/
OHDSI Observational Health Data Sciences and Informatics  https://github.com/OHDSI
VAERS  http://wonder.cdc.gov

**Student Evaluation & Grading:**

*Group Discussions and Assignments*---Current drug safety issues. The purpose of the case studies is to help students relate materials taught in lectures and discussed in the problem-based learning group sessions to an important issue in drug safety. Each student is required to submit a 1-page single spaced summary of the major issues involving this case. Student will be chosen randomly to lead the discussion. Due dates for submission and assignment will be posted through Sakai.

*Research Topic*---A one-page outline of the topics should be submitted by **Feb 10th** for approval, the format of the protocol should conform to the NIH guidelines. It should include the sections: abstract; aims, background; preliminary studies; and methodology. The methodology should include variable definitions, level of measurement, power analysis, research design, and a data analysis plan. The length of protocol should not exceed 6 pages (single spaced). This protocol is due **April 20th**. Additionally, each of you will present your protocol in the power point format. More details and the schedule are listed below.
Final Exam --- The final exam covers the lecture materials, readings, and group activities planned throughout the course.

Late Assignment Policy:
Assignments are due at the beginning of the stated class period. The final manuscript is due at 5:00 PM on the indicated date. Late papers will receive either: (1) the class mean, if the actual score is the mean or higher or (2) the actual score, if the score is lower than the class mean. Delays due to unforeseen and distressing events (serious illness, a death in the family, computer hardware/software failure, etc.) will be treated on a case-by-case basis by the course coordinator.

Grading Scale:
A total of 100 points are possible in this course. Weights will be assigned to the required assignments in the following manner:
Current event/Participation--- 20 points (write up: 15; discussion: 5)
Research Topic --- 40 points (protocol write-up: 30; presentation: 10)
Final exam--- 40 points

Your scores from each of the assignments will be combined to calculate your total score. Final grades will be assigned according to the following scheme:

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Grade</th>
</tr>
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<tbody>
<tr>
<td>95-100</td>
<td>A</td>
</tr>
<tr>
<td>90-94</td>
<td>A-</td>
</tr>
<tr>
<td>86-89</td>
<td>B+</td>
</tr>
<tr>
<td>83-85</td>
<td>B</td>
</tr>
<tr>
<td>80-82</td>
<td>B-</td>
</tr>
<tr>
<td>76-79</td>
<td>C+</td>
</tr>
<tr>
<td>73-75</td>
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<tr>
<td>70-72</td>
<td>C-</td>
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<tr>
<td>66-69</td>
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<tr>
<td>63-68</td>
<td>D</td>
</tr>
<tr>
<td>&lt;60</td>
<td>E</td>
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Student Responsibility and Participation:
Students are responsible for preparing all assigned readings prior to the lecture. Readings should be brought to class on the day they will be discussed. Students are also encouraged to bring to the attention of the instructor and other class members relevant items of interest.

Academic Dishonesty
Familiarize yourself with the University's policy regarding academic dishonesty. See the Statements regarding the Student Conduct Code in the 2008-2009 Graduate Catalog. This policy will be strictly enforced. The University's conduct regulations are available on the Internet at [http://oss.ufl.edu/stg/](http://oss.ufl.edu/stg/). Please note that the course instructors will closely examine your paper submissions for plagiarism. Please review your notes from our orientations session about academic dishonesty and make sure that you understand the steps needed to avoid plagiarism.

Accommodations for Students with Disabilities
Students requesting classroom accommodation must first register with the dean of Students Office. The Dean of Students Office will provide documentation to the student who must then provide this documentation to the Instructor when requesting accommodation.
Course Schedule:

1/6: Course overview; introduction of terminology; role of pharmacoepidemiology in the regulatory agencies, drug industry and academe. Review of major methodologies.
- Chapter 1. AG Hartzema, HH Tilson, KA Chan. The Contribution of Pharmacoepidemiology to the Study of Drug Uses and Effects, and Risk Management.
- Chapter 2. Robert F. Reynolds Epidemiology in Drug Development

1/13: Drug approval process; PDUFA; NDA; BLA: ANDA; branded versus generics; biological, and orphan drugs
- PDUFA IV: [http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm](http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm)

1/20: Pharmacovigilance; MedWatch; EMEA; Pharmacovigilance; Spontaneous Reporting Systems. **Lead: Adel Alrwisan**
- Chapter 5. Ahmad SR, Quellet_Hellstrom, McClosky CA. Pharmacovigilance.
- Chapter 6. Shakir SAW. Prescription Event Monitoring in the United Kingdom

1/27: Active drug safety surveillance; life cycle of the drug; market penetration; sequential analysis

2/3: Data mining; disproportionate analysis. **Lead: Irene Murine**
2/10: **Drug Utilization studies**
- Chapter 7. Wettermark B. Drug Utilization research.
- Chapter 8. Haaijer-Ruskamp FM. Prescribing Quality Indicators.

2/17: **Safety trials / Cohort studies.** *Lead: Chintan Dave*

2/24: **Case-control, nested case-control studies; and matching in pharmacoepidemiology**
- Chapter 18. Rawson NSB, Shatin D. Assessing the validity of diagnostic data in large administrative healthcare utilization databases.
- Chapter 32. Lewis MA. Advanced Pharmacoepidemiologic Reasoning: The story of second and third generation oral contraceptives.

3/2: **Spring Break**

3/09: **Health Outcomes of Interest Definitions in Claims and Electronic Health records.**
**Broader versus wider definitions. Sensitivity and Specificity of Definitions.**
- Carnahan RM, Moores KG. Mini-Sentinel's systematic reviews of validated methods for identifying health outcomes using administrative and claims data; methods and lessons learned. Pharmacoepidemiology and Drug Safety 2012;21(S1): 82-89.

3/16: **Confounding and propensity scores, and other strategies to address confounding.**
*Lead: Ayad Ali*
Chapter 11. Schnweiss S. Confounding

3/23: **Misclassification /Biases.** *Approaches to Bias reduction, sensitivity analysis*
- Chapter 13. AG Hartzema. Addressing misclassification in pharmacoepidemiologic studies.

3/30: **Claims versus Electronic Health Records; disparate, federated and centralized data systems**

• Douglas IJ, Evans SJW Clopidogrel and interaction with proton pump inhibitors: comparison between cohort and within person study designs. BMJ 2012;345:e4388 doi: 10.1136/bmj.e4388 (Published 10 July 2012)
• Maclure M, Fireman B. When should case-only designs be used for safety monitoring of medical products? Pharmacoepidemiology and drug Safety 2012;21(S1); 50-61.

4/13: Patient registries; device epidemiology.
• Chapter 16. DL Covington. Pregnancy registries.

4/20: (last day of classes): Therapeutic risk management strategies, evaluation of therapeutic risk management strategies/ good pharmacoepidemiology practices

Final Exam; Exact Date and time to be determined. Final Exams April 23-29.

Protocols are due on April 20th at 5:00 PM. Please do not submit your protocol as PDF files.

Important Deadlines:
• Current events write-up due: Monday prior (all)
• Current event discussion: Wednesday (presenter)
• Research topic due: Feb 10th (all)
• Research topic power point due: Monday prior (presenter)
• Research topic presentation: Wednesday (presenter)
• Research topic protocol write up due: April 20th (all)

Current Events:

In the first part of the semester, we will have 8 current event topics sessions. The topics will be selected and provided by your instructor on Mondays (2 weeks before the due date). Everyone
will be required to submit a 1-page write-up on Monday of the assignment week. On Wednesdays of that week, a person assigned as a presenter will lead the discussion on the selected topic. We will use the last hour of the class for the discussions. Everyone is expected to come prepared and participate.

**Current Events Schedule**

<table>
<thead>
<tr>
<th>Session</th>
<th>Date</th>
<th>Write-up Due</th>
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<tbody>
<tr>
<td>1</td>
<td>13-Jan</td>
<td>11-Jan</td>
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<tr>
<td>2</td>
<td>27-Jan</td>
<td>25-Jan</td>
</tr>
<tr>
<td>3</td>
<td>3-Feb</td>
<td>1-Feb</td>
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<td>To be decided</td>
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**Research Topic Presentations:**

In the second part of the semester, we will have 4 sessions of presentations. You will present the research topic you selected. Everyone will be required to submit the power point presentation on Tuesday of the presentation week. On Wednesdays of that week, a person assigned to present will have 15-min presentation, followed by 10 mins Q&A. We will use the last hour for the presentations. Everyone is expected to participate.

**Presentations Schedule CHANGE DATES**

<table>
<thead>
<tr>
<th>Session</th>
<th>Presenter</th>
<th>Power Point Due</th>
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<tbody>
<tr>
<td>30-Mar</td>
<td>Yasser Albogami</td>
<td>29-Mar</td>
</tr>
<tr>
<td>6-Apr</td>
<td>Cheng “Alice” Chen</td>
<td>5-Apr</td>
</tr>
<tr>
<td>13-Apr</td>
<td>Guanming Chen</td>
<td>12-Apr</td>
</tr>
<tr>
<td>20-Apr</td>
<td>Omotola Olasupo</td>
<td>19-Apr</td>
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</tbody>
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The instructor reserves the rights to update any part of syllabus as necessary. Students will be notified of any changes.